REMARKS/ARGUMENTS

Status of the specification:

The specification has been amended to correct the reference to the McCormack art cited in paragraph 10 of the instant application. The original specification referred to this art as Hayes et al. and, accordingly, has been corrected here as McCormack et al. Applicants respectfully submit that no new material has been added as the original reference was otherwise correct except that it named the second author, Hayes, instead of McCormack.

Status of the claims:

Upon entry of the present amendment, claims 1-3, 5, 6, and 11 will be pending in the application and presented for examination. Claims 2 and 3 are presented in original form. Claim 1 has been amended to set forth a preferred embodiment, namely methods of preventing infections from infectious agents having a lipid bilayer. Further, claim 1 has been amended to clarify that the lipid moiety of the single chain lipid active agent is functionally required for prevention of the infection. Support for this amendment can be found, for example, in originally presented claims 5, 7, and 9 being drawn to enveloped viruses, bacteria, and parasitic protozoans. Claims 5 has been amended to update dependency. Claim 6 has been amended to update the recital of virus to enveloped virus. Claim 11 has been amended as to no longer claim mucosal and dermal formulations. Applicants respectfully submit that no new material has been added.

I. Rejections Under 35 U.S.C. §112

1. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-6 and 11 stand rejected for an alleged lack of enablement for generic 'single chain lipid active agent' and prevention of infection. Applicants respectfully traverse this rejection. In an honest attempt to expedite prosecution, Applicants have amended pending independent claim 1 to recite "wherein the lipid moiety of said single chain lipid active agent is required for prevention of said infection; and, wherein said infection is caused by an infectious agent having a lipid bilayer." As such, Applicants submit that the claims are no longer subject to the above rejection and are in condition for allowance.

As the Examiner points out, the Forman factors dictate whether a disclosure meets the enablement requirements of 35 U.S.C. §112, first paragraphs. These factors include (i) the relative skill of those in the art; (ii) the nature of the invention; (iii) the breadth of the claims; (iv) the amount of guidance presented; (v) the presence of working examples; (vi) the state of the art; (vii) the predictability of the art; and (viii) the quantity of experimentation necessary. *Ex parte Forman*, 230 U.S.P.Q. 546 (PTO Bd. Pat. App. & Inter. 1986), *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Applicants first review the claims and then address these factors as raised by the Examiner. A general summary of the analysis is presented at the conclusion of these remarks.

The rejected claims have been amended to recite methods of using single chain lipid active agents for preventing infections caused by infectious agents having a lipid bilayer. As such, Applicants respectfully assert that any person skilled in the art to which the invention pertains, or with which it is most nearly connected to, is enabled to use the claimed 'single chain lipid active agent' commensurate in scope with the claims as amended.

(i) Nature of the Invention: The invention is drawn to methods for preventing an infection from an infectious agent having a lipid bilayer by using a liposomal formulation of a single chain lipid active agent.

(ii) State of the Prior Art: Applicants agree with the Examiner that the state of the prior art is very high for formulating liposomal compositions containing specific drugs for the treatment of disease. However, Applicants also submit that the state of the prior art is very high for treating different diseases, sharing a common feature, with the same drug. For example, TNF-α blockers are used to treat a number of different diseases including, but not limited to, rheumatoid arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis, Crohn's disease, and ulcerative colitis. As amended, independent claim 1 recites methods for treating infections caused by agents having a lipid bilayer, the common feature being exploited in the current invention.

(iii) Relative Skill of those in the Art: The relative skill of those in the art is very high, and it is commensurate with Ph.D. level technology as admitted by the Examiner.

(iv) Predictability of the Art: The general predictability of formulating liposomally encapsulated compositions is very high as admitted by the Examiner. However, Applicants respectfully disagree with the Examiner's analysis of the lack of predictability when using an effective drug on a novel target. Evidence of such predictability can again be found in the use of TNF-α blockers in the treatment of various diseases sharing a common feature. As in the use of TNF-α blockers, which target over-induced inflammatory responses, the instant invention exploits a common feature, namely the lipid bilayer, shared by the infectious agents. The Examiner uses the example of a drug-resistant tuberculosis strain as evidence for his argument. Applicants respectfully contend that this example is not material as these drugs target essential tuberculosis proteins, as opposed to lipid bilayers as in the instant invention. The cited drug resistance is achieved by introducing mutations in the targeted proteins, resulting in reduced binding affinities for the drugs. This is not the case in the instant invention, as lipids are not encoded by genomic material. Furthermore, the Examiner cites the Zips art as allegedly evidencing that in vitro studies may or may not be enough to predict a compound's effect in vivo. This reference is also immaterial as it is drawn to studies of anticancer agents, which target proteins and nucleic acids, but not lipid structures.

(v) Breadth of the Claims: Applicants have amended independent claim 1 to recite "wherein said infection is caused by an infectious agent having a lipid bilayer." As such, the claims are now sufficiently narrow to only encompass the prevention of infections caused by agents sharing the common exploited feature, lipid bilayers. The Examiner alleges that since RNA and DNA viruses each act by different mechanisms at any time, it would be impossible to determine when the individual will be exposed to any specific microbial agent and prevent such subsequent infection. However, Applicants contend that since all relevant DNA and RNA viruses are encapsulated at the point of infection, Applicants submit that said viruses would necessarily be exposed to the inventive formulations at the point in time in which an infection would occur.

(vi) Amount of Guidance Provided: The amount of guidance provided by the specification is high. The specification teaches preferred liposomal formulations, for example, at paragraphs [0029] to [0034]. The specification teaches preferred active agents, for example, at

paragraphs [0035] to [0044]. The specification teaches additional agents which can be used in conjunction with the current invention, for example, at paragraphs [0045] to [0046]. The specification teaches modes of administration, for example, at paragraphs [0047] to [0056]. The specification teaches the construction of liposomes, for example, at paragraphs [0057] to [0065]. The specification provides examples of liposomal formulations that are effective in killing gonococcus, HSV-1, HSV-2, and HIV in Examples 1 and 2 at pages 16 to 18. The specification provides an example of administration of a liposomal formulation in Example 3 at pages 18 to 19. As evidenced above, the specification provides ample guidance to practice the invention commensurate in scope with the amended claims.

(vii) Presence of Working Examples: As evidenced above, the specification provides examples of the efficacy of a single chain lipid active agent, octylglycerol, for killing several infectious agents containing lipid bilayers, i.e., gonococcus, HSV-1, HSV-2, and HIV. These examples evidence that single chain lipid active agents can kill representative agents as recited in the amended claims.

(viii) Quantity of Experimentation Necessary: As stated previously, the claims have been amended to recite methods for preventing specific infections being caused by agents containing lipid bilayers are now claimed. Accordingly, and in light of the examples described above, undue experimentation would not be needed in order to practice the invention commensurate in scope with the amended claims.

Conclusion: In light of the current amendments to the claims and the above analysis of the Forman factors, Applicants respectfully submit that any person skilled in the art to which it pertains, or with which it is most nearly connected to, is enabled to use the claimed 'single chain lipid active agent' commensurate in scope with these claims. As such, Applicants respectfully request that this rejection be withdrawn.

2. Rejection Under 35 U.S.C. §112, Second Paragraph

Claim 11 stands rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. In an earnest attempt to expedite prosecution, Applicants have amended claim 11 to remove the recitals of mucosal and dermal formulations. As such, Applicants submit that

claim 11, as amended, is no longer indefinite and respectfully request that this rejection be withdrawn.

II. Rejections Under 35 U.S.C. §102(b)

1. First Rejection Under 35 U.S.C. §102(b)

Claims 1-6 and 11 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Hostetler et al. (US 2001/0033862). Applicants respectfully traverse the rejection. Hostetler et al., while disclosing lipid derivatives of "nucleoside analogues having antiviral activity" (see, lines 2 to 5 of the Abstract), do not teach lipid active agents for preventing infections resulting from infectious agents having lipid bilayers. The lipid derivatives in Hostetler, as evidenced by the Abstract, *"are effective in improving the efficacy of antiviral nucleoside analogues by prolonging the antiviral activity after the administration of the drug has ended..."* As such, the Hostetler art teaches antiviral compounds that work by inhibiting viral polymerases with nucleoside analogue active agents and not by targeting the lipid bilayer with single chain lipid active agents, as in the instant application. Furthermore, the compounds taught in the Hostetler reference would not serve to prevent infection, as polymerase action is not necessary for this step. As such, the Hostetler reference fails to teach methods for preventing infections with or without single chain lipid active agents. Therefore, Applicants respectfully request that the above rejection be withdrawn.

2. Second Rejection Under 35 U.S.C. §102(b)

Claims 1-2, 4-5, and 11 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Spevak et al. (J. Am. Chem. Soc, 1993). Applicants respectfully traverse the rejection. Spevak et al., while disclosing lipid derivatives of *O*-sialosides, do not teach single chain lipid active agents, wherein the lipid moiety of said single chain lipid active agent is required for preventing infections resulting from infectious agents having lipid bilayers. The lipid derivatives taught in Spevak et al. act though *O*-sialoside binding to hemagglutinin, as evidenced by lines 1-5 of column one on page 1146:

> *The surface lectin of the influenza virus, hemagglutinin, binds to terminal α-glycosides of N-acetylneuraminic acid (NeuAc) on cell-surface glycoproteins and glycolipids. Viral binding to cells expressing terminal*

NeuAc residues can be inhibited by α-O-glycosides of NeuAc (O-sialosides).

As such, Spevak et al. teach the functional use of O-sialosides and merely use the lipid derivation to aid in delivery. This is in stark contrast to the instant application, which teaches the use of single chain lipids as the active agent to prevent infections. As such, Applicants respectfully request that the above rejection be withdrawn.

III. Rejection Under 35 U.S.C. §103(a)

Pending claims 1-6 and 11 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Eibl (US 2002/0173489) in combination with Ho et al. (US 2004/0208921), Hostetler et al. (US2001/0033862) and Firshein (U.S. Patent No. 6,121,245), individually or in combination. In this regard, the Examiner alleges that Eibl teaches formulations containing single chain lipids for infections such as HIV. The Examiner further alleges that Ho et al., Hostetler et al., and Firshein teach the use of liposomes as delivery agents for such drugs. Applicants respectfully traverse this rejection.

NO PRIMA FACIE CASE OF OBVIOUSNESS EXISTS

Applicants respectfully point out that the currently amended claims are focused on methods of using single chain lipids as active agents in liposomal formulations for the *prevention of infection* resulting from infectious agents having lipid bilayers, and assert that a *prima facie* case of obviousness has not been established for the presently claimed invention. To establish a *prima facie* case of obviousness, 3 basic criteria must be met:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that a *prima facie* case of obviousness has not been established because there is no suggestion or motivation to modify the cited reference; and the cited references do not teach all the claimed limitations.

There is No Suggestion or Motivation to Modify the Cited References.

Applicants state that there is simply no motivation or suggestion provided in the cited references to modify their teaching in the way the Examiner has contemplated. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

As amended, the claims are drawn the use of a liposomal formulation comprising single chain lipids as the active agent for preventing infections resulting from agents having lipid bilayers. Specifically, the presently claimed method, as set forth in amended independent claim 1, recites:

> **1.** (currently amended): A method for preventing an infection in a mammal, said method comprising: administering a pharmaceutically effective amount of a liposomal formulation to said mammal, wherein said liposomal formulation comprises:
>
> a) a lipid vesicle; and
>
> b) at least one single chain lipid active agent,
>
> wherein the lipid moiety of said single chain lipid active agent is required for prevention of said infection; and,
>
> wherein said infection is caused by an infectious agent having a lipid bilayer.

Applicants respectfully assert that none of the cited references teach or suggest using a single chain lipid active agent, wherein the lipid moiety of said single chain lipid active agent is required for prevention of said infection. In stark contrast to the present invention, the Eibl reference teaches "compounds and compositions (that) are particularly useful in the *treatment of conditions* involving viruses with a lipid membrane" (see, paragraph [0089]). And

more specifically, the use of "therapeutic compounds having activity as a biological response modifier, which are especially suitable for the treatment of tumors" (see, paragraph [0002]). Biological response modifiers act by altering the effects of the immune-system within the organism being treated. As such, these compounds would not be effective in preventing infections as they rely on modifying a host's immune response, which would be activated only after infection. Conversely, the formulations taught in the instant application do not rely on the host organism, as evidenced by examples 1 and 2, which show activity *in vitro*. This is advantageous, as initial infection occurs rapidly after exposure to an infectious agent. Since the Eibl art teaches *treating conditions* caused by viruses through modifying the immune response of the host organism, and not *preventing infections* by directly targeting the infectious agent, Applicants respectfully assert that there is no motivation to modify the reference in such a way as the Examiner has contemplated.

The Prior Art References when Combined Do Not Teach or Suggest All the Claim Limitations.

Applicants state that the cited references do not teach or suggest all of the limitations of the instant claim, as currently amended. Obviousness can only be established when the prior art or combination of prior art teaches or suggests all of the claim limitations. The Eibl reference, as outlined above, does not teach the use of single chain lipid active agents, wherein the lipid moiety of said single chain lipid active agent is required for the prevention of infection. Similarly, Hostetler et al., as outlined in the arguments against the first rejection under 35 U.S.C. §102(b) above, also fail to teach the use of a lipid moiety in the prevention of infection. Furthermore, neither the Ho et al. nor the Firshein references supplement this deficiency. Firshein, while teaching that alkylglycerols can be administered in liposomal formulations, is drawn to methods for treating malignant tumors and not for preventing infections. Finally, Ho et al., as admitted by the Examiner, disclose liposomal formulations of drugs for targeted delivery to lymphoid tissues. However, Ho et al. do not teach the use of single chain lipid active agents for the prevention of infections. Therefore, as this reference also fails to supplement the deficiencies of the Eibl art, the combination of the cited references fails to teach

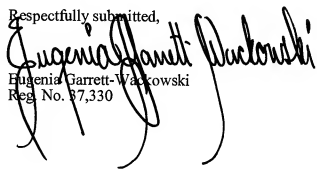
or suggest all the claim limitations of the instant claims. As such, Applicants assert that no *prima facie* case of obviousness exists and respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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